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RAT AA-26: BEHAVIORAL PHARMACOLOGY SCIENCE PIONEER

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Rat AA-26, despite 1950s "state of the art," nonetheless generated the first set of behavioral pharmacology cumulative records to appear in the weekly journal *Science,* the century-old publication of the American Association for the Advancement of Science. The laboratory exploits of this dedicated animal called early attention to the methodological fruits of a marriage between pharmacology and the experimental analysis of behavior.

Key words: conditioned emotional response, conditioned suppression, reserpine, amphetamine, conflict, minor tranquilizers, lever press, rat

Because this special issue on behavioral pharmacology documents on impressive record of research progress over the past four decades, it seems fitting to acknowledge the contributions of one of our earliest science pioneers. In the best tradition of a behavioral analysis of drug action with an emphasis on the behavior of individual organisms, this humble rodent, Rat AA-26, set the standard that was the hallmark of the "Call for Papers" to which the present volume is eloquent response. No matter that this single animal's postdrug performances revealed little in the way of dose–effect relationships, duration of drug action, or historical interactions. Suffice it to recall that Rat AA-26, despite 1950s "state of the art," nonetheless generated the first behavioral pharmacology cumulative records to appear in the weekly journal *Science,* the century-old publication of the American Association for the Advancement of Science.

The succinct and meaty story told by Rat AA-26 was certainly not the first account of drug–behavior interactions to grace the venerable pages of *Science,* but the laboratory exploits of this dedicated animal called early attention to the methodological fruits of a marriage between pharmacology and the experimental analysis of behavior. What the reported contrasting behavioral effects of reserpine and amphetamine upon the rat's "emotional" repertoire may have lacked in scientific rigor was more than compensated for by the "honeymoon fervor" that accompanied an enduring and productive union.

The "typical" cumulative record of the proverbial "typical" animal was of course our stock in trade in those early days. Figure 1, reproduced from the original *Science* paper (Brady, 1956), epitomizes this spartan approach to a behavioral analysis of drug action. The top saline control record shows the marked *decrease* in water-rewarded lever pressing during a 3-min clicker presentation—the short offset sections of the cumulative record between the two arrows—immediately preceding foot shock (broken arrow) in the absence of drug. Amphetamine, shown in the middle section of the figure, accentuated this suppressing effect of the conditioned "anxiety" procedure by *increasing* the lever pressing rate *between,* and *decreasing* even further the rate of lever pressing *during,* clicker presentation. Reserpine, in contrast, had precisely the opposite effect, as shown in the lower section of Figure 1, *decreasing* the lever pressing rate *between,* and *increasing* the rate *during,* clicker presentations.

Parametric shortcomings notwithstanding, the findings with this solitary animal were subsequently replicated in a published experiment with 3 additional rats and a monkey (Brady, 1959). Of at least equal import was the demonstration that reserpine, despite its attenuating effect upon such conditioned "anxiety" (even Skinner and Estes talked funny!), had no effect upon a topographically similar "conditioned suppression" (Hunt & Brady, 1955) produced by punishment of lever responses (electric foot shock) during 3-min clicker presentations. It was this latter procedure that made Irv Geller famous. A noteworthy con-

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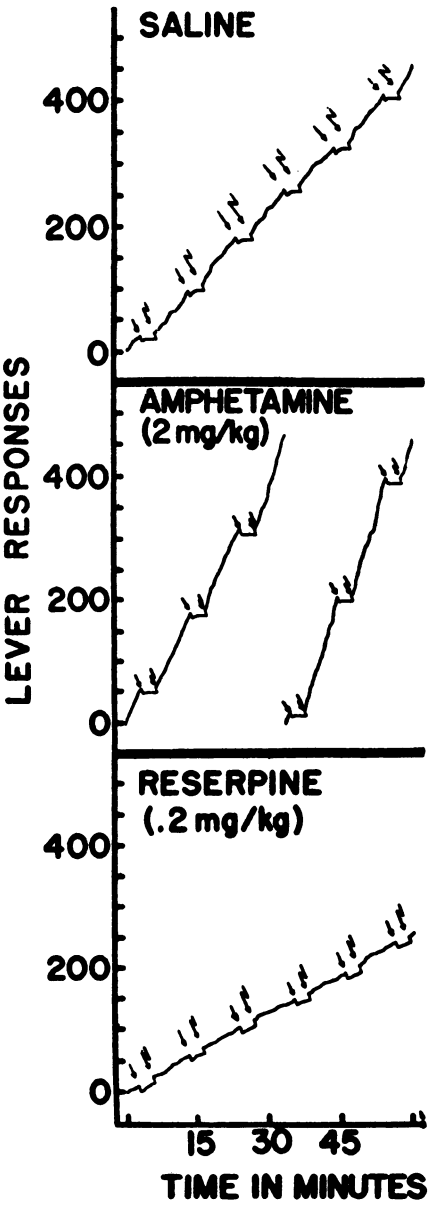

Fig. 1. Sample cumulative-response curves for Rat AA-26 showing the effect of amphetamine and reserpine on lever pressing and on the conditioned emotional response. The oblique solid arrows indicate the onset of the conditioned auditory stimulus, and the oblique broken arrows indicate the termination of the conditioned stimulus contiguously with the brief unconditioned grid-shock stimulus to the feet.

tributor to the saga of Rat AA-26 (see footnote to the 1956 *Science* paper), Irv took the punishment methodology all the way to Philadelphia, made some creative changes in the procedure, renamed it "conflict," and soon published (Geller & Seifter, 1960) one of the most significant behavioral pharmacology contributions to the preclinical evaluation of the so-called "minor tranquilizers."

It is tempting to recall the rapid development of behavioral pharmacology research initiatives in virtually every major pharmaceutical company laboratory following the published exploits of Rat AA-26. But a contingency, even a well-defined temporal ordering of stimulus and response events, is not a dependency, and there is no need for overreaching claims to enhance the contributions of our behavioral pharmacology *Science* pioneer.

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